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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,535	08/26/2005	Lorne J Brandes	3172-103	5333

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
06/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/526,535	BRANDES, LORNE J	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-19 is/are rejected.

7)☒ Claim(s) 1-19 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/31/2005.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 03/11/2005 has been received and acknowledged.

Status of Claims

Claims 1-19 are pending and are examined in this office action.

Specification

The specification of the disclosure is objected to because (i) page 1 not numbered) and (ii) contains trademark . The use of the trademark has been noted in this application (see page 6 and 7 for example). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims1-19 are objected to because of the following informalities: the gap within the formula in claim 1 makes the diphenyl formula unclear as to what diphenyl compound structure is meant. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "sufficient time to permit" for example in claim 1, item b, line 1 is not defined by the claim, the specification does not provide a standard for ascertaining the requiste degree. For example what is meant by a sufficient time to permit? Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. How to determine what time is sufficient to permit inhibition of binding of intracellular histamine, subsequently administering to the patient an anthracycline chemotherapeutic agent and a taxane chemotherapeutic agent as in claim 1 for example.

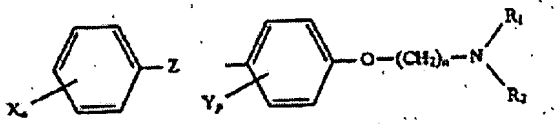
Claim Rejections - 35 USC § 103

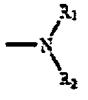
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims **1-19** are rejected under 35 U.S.C. 103(a) as being unpatentable over Brandes US 5,618,846 taken with Vincent 2004/0248986 and Khoo et al. *Journal of Clinical Oncology*, Vol 17, Issue 11 (November), 1999: 3431-3437(submitted IDS) in view of Beer et al. The prostrate 45: 184-193 (2000).

With regards to the instant claim 1 the Brandes reference teaches a chemotherapeutic treatment of cancer cells- inflammatory breast cancer (all tumors are inflammatory (see col. 12, lines 53 and col. 11, line 60-61) comprising administering the



a diphenyl compound (DPPE) (see col. 3, lines 10-15) as in the instant claim 1, wherein X and Y are each chlorine, Z is an alkylene, from 103 carbon atoms or C=O and R1 and R2 are each alkyl (see col. 3, lines 17-22) followed by a sufficient time (see col. 4 lines 10-13) subsequently administering an anthracycline chemotherapeutic agent (see col. 4, lines 10-13). With regards to claims 2 and 3, the reference teaches  (see col. 3, lines 45-50) having the same substituents as that of the instant claimed invention, wherein the diphenyl is a hydrochloride salt (see col. 3, lines 53-55) as in claim 4. As to the instant claims 5-6 the antracycline chemotherapeutic agent is daunorubicin (see col. 9, Table IV). One of ordinary skill in the art would have been motivated to switch daunorubicin with that of doxorubicin because both are chemotherapeutic drugs from the same family anthracycline, both are used in cancer treatment and would have expected a successful result in doing so. Nothing unobvious is seen in switching one drug that has the same property in the same family with another of the same family. The reference also used adriamycin-which is doxorubicin (see col. 7, lines 40-45).

The Brandes reference further teaches the compound (N, N-diethyl-2-[4-(phenylmethyl)-phenoxy]ethanamine monohydrchloride (DPPE) is administered 30-90 minutes prior to the chemotherapeutic agent (see col. 4, lines 40-42) as in the instant claims 8 and 9-11 and the DPPE is administered intravenously (see col. 5, line 20). The Brandes reference also teaches with regards to claim 8 DPPE is administered prior to administering chemotherapeutic agent DPPE is administered about 8 to 240 mg/M^2 (see col. 4, lines 50-53) wherein the amount is 1-6 mg/kg (see col. 11, lines 10-12) which is within the claim limitation of 3-10 mg/kg as in claims 14 and 15-16. Adriamycin is the registered name for doxorubicin is administered 60 mg/ mg/M^2 (see col. 11, lines 19-20) as in claim 17 in part and 8 and 240 mg/M^2 (see col. 4, lines 50-54) as in the instant claim 13. The reference did not teach the use of a second chemotherapeutic agent, however suggested that the invention is widely applicable to any type of chemotherapeutic drug (see col. 4, lines 25-27). The above reference lacks the teaching of administering the chemotherapeutic treatment in a number of cycles

The term neoadjuvant is meant astreatment that is given first to help make the next treatment step go more smoothly, this type of therapy is mainly used to shrink a large tumor before radiation or surgery as taught by the reference (see abstract) wherein the treatment is carried out to inhibit normal cell proliferation.

Vincent teaches the use of DPPE (see abstract) in a neoadjuvant treatment (as taught having a existing cancer wherein the use of surgery is needed) (see abstract)

DPPE as referred to is the drug compound/formula in claims 1-4. Vincent reference teaches DPPE is administered prior to administering chemotherapeutic

agents intravenously about 30-90 minutes prior to administration (see para. 0100) as in claims 8-11, wherein the anthracycline agent is doxorubicin or epirubicin (see para 0084) and taxane (see 0084) wherein the taxane is paclitaxel or docetaxel (see 0082) as taxol or taxotere as in claims 5-7, thus claim 10 is obvious. The reference further teaches that doxorubicin is administered 60-90 mg as in instant claim 17 (see para 0104) about 20 minutes as in claim 12, wherein the regimen is once for 3 weeks-thus 21 days and number of cycle is from 2-10 which is within the claim limitation of 19 (see para 0104). The reference, however did not teach the taxane is taxol or taxotere, however, the drug family is well known in the art of cancer so using taxane will result in the use of either taxol or taxotere such as paclitaxel or docetaxel (see NCI taxanes in cancer treatment).

Khoo et al. teach administering a DPPE followed by the administration of doxorubicin every 21 days for a maximum of seven cycles which is within the claim limitation of the instant claim 19 (see page 3431 higlighted sec).

One of ordinary skill in the art would be motivated to combine the Khoo et al reference with Vincent and administer the chemotherapy agents in a cycle because administering such agents in a treatment regimen is taught by Khoo et al. Therefore one of ordinary skill in the art would be motivated to do so and expect success because it has been taught by Khoo et al.

Beer et al. teach neodjuvant therapy (see page 186 highlighted sec) in patients undergoing prostectomy, and also the patient population with breast cancer (see page 189, rt. col. highlighted sec), wherein the combination chemotherapy includes the use of

DPPE with taxanes such as paclitaxel and docetaxel. Beer et al also teach administering a taxane taught as (docetaxel or paclitaxel) in the range 75 mg/m^2 (see highlighted sec-pg 187) as in claims 17 and 18. The references use taxol which is paclitaxel as claimed, one of ordinary skill in the art would be motivated to substitute the taxane for taxol or taxotere because taxane, taxol and taxotere belong to a group of chemotherapy drugs and are well known in the art of oncology (see supporting doc. NCI enclosed).

Brandes, lack the teaching of specifically incorporating a taxane, but teaches that any chemotherapeutic agent can be use, thus one of ordinary skill in the art would be motivated to combine the Beer et al., dosage for a docetaxel/paclitaxel. One of ordinary skill in the art would be motivated to use a chemotherapeutic agent use a taxols administer the treatment dosages as taught by both references and expect a successful result because both references teaches the ranges of the drugs and combination is taught by Brandes.

One of ordinary skill in the art would have been motivated to combine the above cited prior art and use a taxol (paclitaxel) as taught by Beer because as taught by Brandes the invention is widely applicable to any type of chemotherapeutic drug (see col. 4, lines 25-27) therefore nothing unobvious is seen in the combination.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made for neoadjuvant chemotherapy in patients with inflammatory breast cancer.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim **1 - 19** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1 - 17** of U.S. Patent Application No. **10526563 in view of Kleer et al**. Breast cancer Res. 2000, 2:423-429) Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

- Both sets of claims refer to adjuvant therapy in treating a subset of cancer (specie) – inflammatory breast cancer in the current application (claims 1 – 19) and metastatic cancer (claims 1 – 17) in the copending application. Inflammatory breast cancer is a cancer that is inflamed and metastasis rapidly. Metastatic cancer is the spreading of the cancer from its origin. An obvious variation of spreading (see Kleer et al page 423 highlighted).

- Both applications recite using the same compositions and/or derivatives thereof. See current application claims 1 - 19 and copending application claims 1 – 17.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Claim **1 - 19** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1 - 21** of U.S. Patent Application No. **10527686 in view of http://www.breastcancer.org/dia_pict_staging.html**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

> Both sets of claims refer to adjuvant therapy in treating cancer – inflammatory breast cancer in the current application (claims 1 – 19) and patients with stage I or II breast cancers (claims 1 – 21) in the copending application. The claims are obvious over each other as inflammatory breast cancer is a cancer that is inflamed and metastasis rapidly. With stage I or II cancer, these stages define how far metastasis have occurred. The current application claims are obvious variation of metastasis of cancer as taught by breast cancer staging stage I desdcribes invasive breast cancer.
>
> Both applications recite using the same compositions and/or derivatives thereof. See current application claims 1 - 19 and copending application claims 1 – 21.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ardin H Marschel 5/12/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

SVG
3/24/07